UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,620	01/29/2007	Maria Sitges Berrondo	251989	9639

23460 7590 08/25/2010

LEYDIG VOIT & MAYER, LTD
TWO PRUDENTIAL PLAZA, SUITE 4900
180 NORTH STETSON AVENUE
CHICAGO, IL 60601-6731

EXAMINER
CARTER, KENDRA D

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
08/25/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Chgpatent@leydig.com

Office Action Summary	Application No.	Applicant(s)	
	10/577,620	SITGES BERRONDO ET AL.	
	Examiner	Art Unit	
	KENDRA D. CARTER	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) *4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Examiner acknowledges the applicant's remarks and arguments of June 4, 2010 made to the office action filed March 4, 2010. Claims 1-4 are pending and amended. Claims 5-8 are cancelled.

The amended claim 4 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the original claims are drawn to a method treating or preventing hearing loss not a method of preventing epileptic seizures. If the presently presented claim 4 was in the original claims the Examiner would have called for an restriction between the two inventions. Particularly, Group I is drawn to claims 1-3, which are drawn to a method of treating or preventing hearing loss associated with epilepsy. Group II is drawn to claim 4, which is drawn to a method of preventing epileptic seizures.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features.

An international application should relate to only one invention or, if there is more than one invention, the inclusion of those inventions in one international application is only permitted if all inventions are so linked as to form a single general inventive

concept (PCT Rule 13.1). With respect to a group of inventions claimed in an international application, unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features.

The expression "special technical features" is defined in PCT Rule 13.2 as meaning those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art. The determination is made on the contents of the claims as interpreted in light of the description and drawings (if any). Whether or not any particular technical feature makes a "contribution" over the prior art, and therefore constitutes a "special technical feature," should be considered with respect to novelty and inventive step.

The common technical feature in all groups is vinpocetine. This element cannot be a special technical feature under PCT Rule 13.2 because the element is shown in the prior art.

In this case, Tigyi et al. (of record) teach vinpocetine (see column 5, lines 25-35 and 55-60). Further, Nekrassov et al. (of record) teach vinpocetine protects from aminoglycoside antibiotic-induced hearing loss in guinea pig in vivo (see title).

As a result, no special technical features exist among the different groups because the inventions in Groups I and II fail to make a contribution over the prior art with respect to novelty and inventive step. In conclusion, there is a lack of unity of inventions, and therefore restriction for examination purposes as indicated is proper.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 4 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

In light of the amendments to the drawings, the objection is withdrawn.

In light of the claim amendments the previous 35 U.S.C. 103(a) rejection is withdrawn and new rejections are below. The new rejections address the claim amendments. In regards to Applicant's arguments that pertain to non-amended claim limitations, the Examiner has addressed them below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Particularly, the recitation of "damage of auditory tract retro-cochlear nuclei" is not in the specification. The specification discloses that vinpocetine cancels all the retro-cochlear abnormalities induced by PTZ or by 4-AP (see paragraph 22) but does not indicated that vinpocetine treats damage of auditory tract retro-cochlear nuclei.

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Particularly, the recitation of “hearing loss of central origin” is not in the specification. The original claims indicated hearing loss of retro-cochlear origin but not specifically of the central origin.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Particularly, the claim is drawn to a method of treating or preventing hearing loss associated with epilepsy, but requires that the amount of vinpocetine is sufficient enough to not only inhibit hearing loss caused by epilepsy but also inhibit auditory tract alterations. The Examiner is not sure if the claim should be a method of treating or preventing hearing loss or a method of inhibiting auditory tract alterations and hearing loss caused by epilepsy. Further there is no subject (i.e. patient) in which the vinpocetine is administered.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Particularly, the claim is drawn to a treating damage of auditory tract retro-cochlear nuclei. The claim is dependent on claim 1, which is drawn to a method of treating hearing loss not damage of auditory tract retro-cochlear nuclei. The Examiner is not clear on what is being treated.

Claim 2 recites the limitation "treating damage of auditory tract retro-cochlear nuclei" in which is dependent on claim 1. There is insufficient antecedent basis for this limitation in the claim. Claim 1 is drawn to a method of treating or preventing hearing loss associated with epilepsy comprising administering an amount of vinpocetine that is

sufficient enough to not only inhibit hearing loss but inhibit auditory tract alterations. There is no mention of “damage” or retro-cochlear nuclei” in claim 1.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Particularly, the claim is drawn to a method of treating hearing loss of central origin, characterized by inhibiting an increase in auditory threshold induced by pentylenetetrazole and 4-aminopyridine. The claim is dependent on claim 1 which is drawn to a method of treating hearing loss associated with epilepsy. The Examiner understands that seizures can be induced with pentylenetetrazole and 4-aminopyridine, but the claim is written such that the “auditory threshold" is increased by these compounds. In other words, the claim should either be drawn to hearing loss of central origin being characterized by the increase of the auditory threshold, or wherein the epilepsy is induced by the claimed compounds.

For compact prosecution, the Examiner has examined claim 1 as a method of treating or preventing hearing loss and inhibiting alterations in the auditory tract associated with epilepsy comprising pre-administering vinpocetine to a patient. The Examiner has examined claim 2 as a method of claim 1, wherein inhibiting alterations in the auditory tract is characterized by inhibition of alterations in amplitude and latency of auditory brainstem response (ABR) later waves. The Examiner has examined claim 3 as a method of claim 1, wherein the

hearing loss is of the central origin and is characterized by the increase of the auditory threshold.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nekrassov et al. (Brain Research, 2000, vol. 868, pp. 222-229) in view of Woolf et al.

(Antimicrobial Agents and Chemotherapy, June 1988, pp. 865-872) and Applicant's admitted art (see specification, page 3, paragraph 9).

Nekrassov et al. teach vinpocetine protects from aminoglycoside antibiotic-induced hearing loss in guinea pig in vivo (see title). Amikacin, the aminoglycoside antibiotic, increases the auditory brainstem response (ABR) at 4 and 8 kHz, but when vinpocetine is administered by i.p. at 2 mg/kg for 13 days after administration of Amikacin, the increase ABR threshold and latency is reduced (see abstract and page 225, section 3.5; addresses claims 1-3) in the first and later waves (i.e. P1, P3 and P4 in fig. 1; addresses claim 2).

Nekrassov et al. do not teach that the hearing loss is associated with epilepsy (claim 1), nor that the patient is pre-administered vinpocetine (claim 1). Nekrassov et al. also does not specifically teach that the hearing loss associated with epilepsy is of the central origin.

Woolf et al. teach that ganciclovir administered 1 day before inoculation of cytomegalovirus labyrinthitis protect the cochlea from the histopathologic changes and hearing loss normally associated with cytomegalovirus labyrinthitis (see abstract).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the teachings of Nekrassov et al. and to treat hearing

loss that is associated with epilepsy (claim 1) because Nekrassov et al. teach the treatment and prevention of hearing loss at 4 and 8 kHz with the Applicant's claimed compound. Thus, regardless of the cause, hearing loss is still treated. One would be motivated to try a treatment for hearing loss regardless of its cause, especially if the hearing loss was treated.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the teachings of Nekrassov et al. and treatment wherein the patient was pre-administered vinpocetine because of the following teachings: 1) Nekrassov et al. teach the treatment and prevention of hearing loss at 4 and 8 kHz with the Applicant's claimed compound; 2) Woolf et al. teach that prophylactic administration of ganciclovir protect the cochlea from the histopathologic changes and hearing loss normally associated with cytomegalovirus labyrinthitis (see abstract). Although the teaching of Woolf et al. is for a viral infection, Woolf et al. provides evidence that prophylactic administration of a drug to protect against hearing loss is known. Since it is known in the art that antiepileptic drugs result in hearing decline (see Applicant's specification page 3, paragraph 9), one skilled in the art would be motivated to try prophylactic administration of vinpocetine to prevent or reduce hearing loss.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the teachings of Nekrassov et al. and wherein the hearing loss associated with epilepsy is of the central origin characterized by inhibiting

an increase in auditory threshold because the Nekrassov et al. teach that vinpocetine reduced the increase of the ABR threshold and latency (see abstract and page 225, section 3.5). Thus, since vinpocetine reduces increased auditory threshold and hearing loss, then it obviously is of the central origin.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive.

> The Applicant's argues that the aminoglycoside studies of Nekrossov et al. and Hotz et al. invariable involve alterations in the most peripheral generators of the first wave of the ABR. The reverse is not true for ABR wave alterations associated with epilepsy, i.e., changes in the later ABR waves associated with epilepsy. It is impossible to predict that the same drug of Nekrassov et al. (i.e. vinpocetine) could be useful to prevent hearing loss of such a different etiology. The Applicant further argues that the Examiner can not use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.

The Examiner disagrees because first the claims are drawn to the treatment and prevention of hearing loss associated with epilepsy. Second, when vinpocetine is administered by i.p. at 2 mg/kg for 13 days after administration of Amikacin, the increase ABR threshold is reduced (see abstract and page 225, section 3.5) in the first

and later waves (i.e. P1, P3 and P4 in fig. 1; addresses claims 2 and 3). In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KENDRA D. CARTER whose telephone number is (571)272-9034. The examiner can normally be reached on 9:00 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kendra D Carter/
Examiner, Art Unit 1627

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1627